

## Why research sex differences and similarities?

Women's health has benefited from the contributions of medical physicists, such as the development of novel imaging methodologies to improve breast cancer detection rates. Though women's health research is sometimes thought to be synonymous with the study of diseases such as breast and ovarian cancer and those that affect reproductive health, it is in fact a much more encompassing field and the study of health and disease in both the sexes is critically important to advancing women's health.

Sex differences research is a science that entails comparing and contrasting scientific data between the sexes in order to understand how these factors affect health. The goal is to learn how basic biologic mechanisms, disease manifestations, and therapeutic responses may be similar or different in women and men so that targeted, tailored and highly effective prevention, diagnostic, and treatment strategies may be developed. Sex differences research, therefore, has the power to benefit both men and women, by informing the delivery of more personalized, sex-appropriate care.

Because it is such an important area of study, the National Institutes of Health (NIH) Strategic Plan for Women's Health and Sex Differences Research includes two goals on this topic. They are to increase sex differences research in basic science studies, and to incorporate findings of sex/gender differences in the design and application of new technologies and medical products. Additionally, the NIH Office of Research on Women's Health (ORWH) funds several Specialized Centers of Research on Sex and Gender Factors (SCORs) to conduct sex differences research. The centers conduct interdisciplinary research focusing on sex differences through an integrated basic, clinical, and translational research approach. A recent study<sup>1</sup> from one SCOR used functional MRI to assess responses to stress in cocaine-dependent women and men as well as comparison subjects. The study found that corticostriatal-limbic hyperactivity appears to be linked to stress cues in women, drug cues in men, and neutral-relaxing conditions in both (cocaine-related neuroadaptations in corticostriatal-limbic circuits may underlie behavioral and cognitive aspects of cocaine dependence). The authors concluded with the suggestion that sex should be taken into account in the selection of therapies in the treatment of addiction, particularly those targeting stress reduction.

This example highlights the clinical relevance of sex differences research, and how findings may lead to sex-appropriate therapies and medical care. The value of sex differences research has also been studied by the Institute of Medicine. In 2010, a workshop was held entitled "Sex Differences and Implications for Translational Neuroscience Research." Participants offered recommendations that included funding ba-

sic and clinical interdisciplinary research to "establish the scientific basis for sex differences in health and neurological disease," and to "...build predictive and translatable models of human neurological disease and identify potential biomarkers."<sup>2</sup>

While those recommendations are specific to neuroscience, it is important to note that a sex differences approach can be applied across the research continuum (from basic to clinical and translational research) and in a variety of scientific disciplines including medical physics and biomedical engineering. In fact, the U.S. Food and Drug Administration (FDA) has recently issued a draft guidance on the evaluation of sex differences in medical device clinical studies (see list of resources below for details). By simply considering sex as a biologic variable when designing a study and analyzing and reporting the results by sex, where appropriate, the value and rigor of the science are vastly enhanced. The potential for sex differences as it pertains to subject selection is also considered with Institutional Review Board review of protocols. Additionally, failing to consider the effects of sex can result in erroneous conclusions, with ramifications ranging from ineffective or suboptimal therapy to outright harm to the patient.

Of note, while considering sex as a basic variable goes a long way toward improving health research, of equal importance is the insistence that data disaggregated by sex, and appropriate sex-specific analyses are published with research findings. This is critical so that the scientific and medical community can further investigate or implement those findings. The Institute of Medicine has also provided commentary on this topic, and at a 2011 workshop, which convened researchers and journal editors, entitled "Sex-Specific Reporting of Scientific Research" four themes for advancing sex-specific reporting were discussed. These included identifying the sex of populations in journal publications (including sex of origin cells and tissues and animals in basic research), sharing of sex-identified raw data to facilitate meta-analyses, "extra credit" in review for manuscripts that include sex-specific information, to enhance a paper's chance of publication, and requiring sex-stratified analyses.<sup>3</sup>

In summary, women's health research involves both the study of diseases and health states that primarily affect women, and also those that affect both women and men. By better understanding the similarities and differences among the sexes that affect health, a more personalized approach to care can be developed to improve health for both men and women. ORWH encourages all researchers to consider sex as a basic biologic variable when developing research questions, designing studies, conducting research, and reporting results.

To learn more about women's health and sex differences research please visit the resources listed below.

## Resources

- NIH Strategic Plan for Women's Health and Sex Differences Research, <http://orwh.od.nih.gov/research/strategicplan/index.asp>.
- Online Courses developed by NIH and FDA on sex differences (CMEs available), <http://sexandgendercourse.od.nih.gov/>:  
 Course 1: The Basic Science and the Biological Basis for Sex- and Gender-Related Differences;  
 Course 2: Sex and Gender Differences in Health and Behavior.
- FDA "Draft Guidance for Industry and Food and Drug Administration Staff—Evaluation of Sex Differences in Medical Device Clinical Studies," <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm283453.htm>.
- Women's Health Resources Web Portal from NIH (one stop shopping for women's health information informed

by research), <http://www.womenshealthresources.nlm.nih.gov/about.html>.

<sup>1</sup>M. N. Potenza *et al.*, "Neural correlates of stress induced and cue induced drug craving influences of sex and cocaine dependence," *Am. J. Psychiatry* **169**, 406–414 (2012).

<sup>2</sup>IOM (Institute of Medicine), *Sex Differences and Implications for Translational Neuroscience Research: Workshop Summary* (The National Academies, Washington, DC, 2011).

<sup>3</sup>IOM (Institute of Medicine), *Sex-Specific Reporting of Scientific Research: A Workshop Summary* (The National Academies, Washington, DC, 2012).

Janine Austin Clayton, MD  
*Office of Research on Women's Health,*  
*National Institutes of Health,*  
 6707 Democracy Boulevard, Suite 400,  
 Bethesda, Maryland 20892-5484  
[Janine.Clayton@nih.gov](mailto:Janine.Clayton@nih.gov)

Stephanie Joseph, MPH  
*Office of Special Health Issues,*  
*US Food and Drug Administration,*  
 10903 New Hampshire Avenue,  
 Silver Spring, Maryland 20993  
[Stephanie.Joseph@fda.hhs.gov](mailto:Stephanie.Joseph@fda.hhs.gov)